HEMOCHROMATOSIS WITH DIABETES MELLITUS.[1]

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The clinical and pathological features of hemochromatosis were presented before this Association in 1899 by Dr. Opie,[2] who reported a fatal case of the disease. Opie's paper gives a complete bibliography of the subject up to the date of publication. At the same meeting, Dr. Osler exhibited a patient who showed some of the leading characteristics of the affection. This case was[3] later published in detail.

There are three cardinal symptoms manifested by hemochromatosis in its most advanced stages: (1) Pigmentation of the viscera, and usually also of the skin; (2) cirrhosis of the liver, almost invariably of the hypertrophic type and accompanied by striking pigmentation of the organ; and (3) diabetes mellitus, which dominates the clinical picture in the latest stage of the disease. The latter is due to the final development of a pigmentary cirrhosis of the pancreas, thus interfering with its glycolytic function.

In Opie's and Osler's cases the disease had not reached the diabetic stage. Death in Opie's case, was precipitated by an attack of typhoid fever. Osler's patient presented a striking pigmentation and had a very large liver. Efforts have been made to trace the course of the disease in the latter case, but the patient has been lost from view. I have the privilege[4] of reporting herewith two fatal cases of hemochromatosis from the medical wards of the Johns Hopkins Hospital, in which diabetes was present and was responsible for the death of the patients. The paper deals only with those cases of hemochromatosis in which the diabetic stage has been reached. In 1899 Anschütz,[5] including one of his own, collected twenty-four cases of hemochromatosis with diabetes. In a review of the literature since that date I have been able to find nine additional cases, which, with the two here reported, make a total of eleven cases reported since 1899. Altogether, therefore, thirty-five cases of hemochromatosis with diabetes have been recorded up to the present time.

Hemochromatosis is a rare disease. In the first seventeen years since the opening of the Johns Hopkins Hospital up to May 15,

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[1] Read at the meeting of the Association of American Physicians, Washington, D. C., May 15 and 16, 1906.

[2] Transactions of the Association of American Physicians, 1899, vol. xiv, p. 253. (For the literature previous to 1899 see the bibliography as given by Anschütz and Opie.)

[3] Brit. Med. Jour., 1899, vol. ii, p. 1597.

[4] I am indebted to Dr. L. F. Barker and Dr. W. S. Thayer for the opportunity of reporting these two cases.

[5] Deut. Arch. f. klin. Med., vol. lxii, p. 411.

1906, there have been only three cases in the medical wards and dispensary, in which, from the clinical features and the finding of hemosiderin in the skin, the diagnosis was without doubt. These cases include Osler's case and the two here reported out of a total of 106,000 medical cases treated in the wards and dispensary. As already stated, only two of these had reached the diabetic stage. That hemochromatosis is an uncommon cause of diabetes is indicated by the fact that it was responsible for the disease in only two instances out of a total of 256 cases of diabetes treated in the medical wards and medical dispensary up to May 15, 1906. The histories of these two cases follow:

CASE I. (*Gen. Hosp. No.* 46430).—*Moderate pigmentation of the face, neck, and hands. Iron demonstrated in the epithelial cells of the sweat glands. Very large liver. Time of onset of pigmentation uncertain. Death from coma twenty months after the onset of the diabetic symptoms.*

E. W. S., male, white, married, aged forty-five years, cigar manufacturer, a resident of Virginia, was admitted to the Johns Hopkins Hospital, April 21, 1904, complaining of "diabetes."

Family History. The only feature of interest was that one brother had died of diabetes at the age of forty-nine.

Personal History. The patient had measles and whooping-cough as a child. Since then the only serious illness was pneumonia at thirty-three. He had gonorrhœa at twenty-five. No lues. Smoked six to ten cigars a day. Previous to two years before admission he had been a heavy drinker, taking from ten to thirty drinks of whiskey daily. His average weight when he was well was 195 pounds.

Present Illness. In January, 1903, the patient began to have marked polyuria and thirst. This was accompanied by increasing weakness and emaciation. He had lost sixty-five pounds since January, 1904. His appetite was ravenous. For three months he had suffered from a general pruritus. Recently a papulosquamous eruption had appeared on the legs and thighs. During the last two months there had been severe cramps in the muscles of the legs. The sexual power had been markedly impaired for a year. Neither the patient nor his friends had been struck by any change in his color.

Physical Examination. The patient was of medium stature and still fairly well nourished. A feature that attracted one's attention at once was a definite but not extremely marked, slaty-brown pigmentation of the face, neck, and hands. The only other situation in which the pigmentation was increased was about the scrotum. In front of the right external malleolus there were three fading purpuric spots. There was no pigmentation of the sclerotics nor of the buccal mucous membrane. No jaundice.

The radial vessels were slightly thickened. The blood-pressure was 123 mm. Hg. The pulse was otherwise normal. The breath possessed a faint, sweetish fruity odor.

The lungs showed signs of slight emphysema. The heart was normal.

The liver was markedly enlarged. The relative hepatic dulness commenced at the middle of the fourth interspace in the mammillary line. The absolute hepatic dulness began at the middle of the sixth rib and extended to a point in the mammillary line 5 cm. below the costal margin and in the median line to a point 14 cm. below the tip of the ensiform cartilage and only 3.5 cm. above the umbilicus. The left lobe of the liver was even more markedly enlarged, its edge disappearing beneath the left costal margin in the anterior axillary line. The edge of the liver was rounded and everywhere well felt. The liver surface was smooth.

The border of the spleen could not be felt. It appeared to be enlarged, however, as its percussion measurements were 10 x 22 cm.

The abdomen revealed a distinct fulness corresponding to the enlarged liver. In the epigastrium there was a properitoneal hernia. There was nothing otherwise to be made out on abdominal palpation. Ascites did not exist.

The deep reflexes were markedly diminished but were still to be elicited. The superficial reflexes were normal.

The ophthalmoscopic examination made by Dr. Mills showed no changes in the fundi.

Blood Count. Red cells 4,800,000 per c.mm.; leukocytes, 7700 per c.mm.; hemoglobin 87 per cent. An examination of a fresh specimen failed to show any evidences of lipemia.

Frequent examination of the stools revealed no excess of fat. Toward the latter part of his stay in the hospital, the patient had an annoying diarrhœa, having from five to ten loose movements daily.

Histological Examination of the Skin. Sections were made by Dr. Opie of a piece of pigmented skin removed from the back of one of the hands, and a marked reaction for iron was found in the epithelial cells of the sweat glands by the potassium ferrocyanide and hydrochloric acid method.

Summary of Urine Examinations. The total amount of urine for the first full twenty-four hours (April 22 to April 23) was 3200 c.c. The urine was clear and of a very pale yellow color. Acid reaction; specific gravity, 1033. No albumin. Sugar, 7 per cent., or 224 grams in the twenty-four hours. There were definite reactions for acetone and diacetic acid, although they were not intense. The microscopic examination was negative.

The patient was put on a non-carbohydrate diet by gradual withdrawal of the starches. After being on a strict diet for nine days he failed to become aglycosuric and was still excreting on the ninth day 75 grams of glucose. As he was losing weight, moderate amounts of starch were allowed. The reactions for acetone and diacetic acid remained positive throughout the patient's entire stay in the hospital.

On May 12, the day before he left the hospital, he voided 1800 c.c. of urine. It was acid; specific gravity 1029; no albumin; sugar, 3.1 per cent. or 55.8 grams; acetone and diacetic acid positive; no casts.

The patient was discharged on May 13, 1904. His condition had not materially changed. The pigmentation had apparently remained about the same. The enlargement of the liver persisted. A clinical diagnosis of hemochromatosis and diabetes mellitus was made.

Dr. J. H. Neff, of Harrisonburg, Va., who had charge of the patient after he returned home, informed me that during the summer a superficial ulcer developed on one of the legs. This slowly healed. There was no special increase in the degree of pigmentation. The patient's condition gradually became worse and he died in coma on September 6, 1904, twenty months after the onset of his diabetic symptoms. Unfortunately no autopsy was obtained.

CASE II. (*Gen. Hosp. Nos.* 52486, *and* 53388).—*Intense pigmentation of many years' standing. Iron demonstrated in the cells of the sweat glands. Enormous liver. Symptoms of diabetes for six months before death. Death from bronchopneumonia and not from coma.*

J. W. S., male, white, married, bricklayer, aged fifty-three years, was admitted to the Johns Hopkins Hospital for the first time on October 6, 1905, complaining of weakness, thirst, and frequent micturition.

Family History. There was nothing of importance bearing on the patient's case.

Personal History. The patient had always been a very healthy man with the exception of an attack of pneumonia seventeen years ago. He denied gonorrhœa and syphilis. He had smoked and chewed tobacco in moderation. Alcohol was used very moderately, three glasses of beer a week. He was the father of eight children. His average weight was 160 pounds.

Present Illness. Six weeks before admission the patient first noticed that he was voiding urine more frequently and in larger amounts, and that he had persistent thirst. These symptoms were preceded for a short time by increasing weakness. During the last four weeks he had lost twenty pounds. His appetite had not been voracious. The bowels were constipated. Six days before admission he had to give up work owing to the increasing physical weakness. For three days he had noticed a diffuse, red eruption over the lower part of the chest, the abdomen, and genitals.

The patient had not noticed any recent change in his color. His daughter said that his skin had been dark for many years and as long as she could remember.

Physical Examination. The patient was fairly well nourished, his weight on admission being 132 pounds. The mucous membranes were of good color. One was immediately struck by the remarkable pigmentation of the skin. This was most marked over the face, neck, and hands, where the skin had a very dark-brown color. The skin of the whole body was much more pigmented than normal, and there was intensification of the color in the axillæ. Over both axillary regions, the lumbar regions of the abdomen, and the groins there was a bright erythema which disappeared on pressure. There was no pigmentation of the sclerotics nor of the buccal mucous membrane. Below the left eye there was a xanthoma plaque measuring about 3 mm. in diameter.

The radial vessels were moderately sclerosed.

The examination of the heart and lungs revealed nothing abnormal.

The liver was enormously enlarged. The relative hepatic dulness commenced at the level of the fourth rib in the mammillary line. The absolute hepatic dulness began at the fifth rib and extended to a point 12.5 cm. below the costal margin in the mammillary line, which was 2 cm. below the level of the umbilicus. In the median line the absolute dulness reached just to the level of the umbilicus. The left lobe was markedly enlarged. The edge of the liver was everywhere readily felt and somewhat rounded. The surface was smooth. The edge of the spleen was easily palpable at the costal margin on deep inspiration. The examination of the abdomen was otherwise negative. There was no ascites.

Both knee-jerks were present but slightly diminished.

Blood Examination. Red cells, 5,304,000 per c.mm.; leukocytes, 9200 per c.mm. Hemoglobin, 95 per cent. (Gowers). The differential count showed no special variations from the normal. There were no evidences of lipemia by either chemical or microscopic tests. On October 9, Dr. Walter Jones examined the blood spectroscopically and reported that only the normal bands of oxyhemoglobin were present.

Microscopic Examination of the Skin. On October 21, a small portion of the skin from the left shoulder was excised to be examined microscopically for iron. The examination was made by Dr. Bunting, who reported as follows: In the Malpighian layer of the epidermis the cells show an excess of fine pigment granules which do not take the Prussian-blue color with the ferrocyanide test. In some of the epithelial cells of the sweat glands and ducts, however, there are present coarser, more refractile granules, which do stain a brilliant greenish-blue and which are granules of hemosiderin. There were no large vessels found giving smooth muscle in which to look for hemofuscin.

Summary of Urine Examinations. For the first full twenty-four hours (October 7 to October 8) 1240 c.c. of urine was voided. It was of amber yellow color; acid; 1034; no albumin; sugar, 4.8 per cent., or 59.5 grams in twenty-four hours; acetone and diacetic acid were present; no casts.

Throughout the patient's stay in the hospital sugar was constantly present, the largest excretion being 272 grams during the twenty-four hours on a mixed diet. The lowest excretion of sugar on a strict non-carbohydrate diet was 39 grams. He failed to become aglycosuric on October 21, when a "hunger-day" was instituted, 23 grams of sugar being excreted. Acetone and diacetic acid persisted in the urine throughout his entire stay in the hospital.

In order to see whether the urine gave any indications of excessive blood destruction it was tested, on October 19, for hematoporphyrin, but the spectroscope failed to give the characteristic absorption bands.

On October 21 the patient was discharged. His general condition had materially improved during his stay in the hospital, and he gained one pound in weight.

Second Admission. The patient was readmitted to the hospital on January 9, 1906. His main symptoms in the interval were a "tired, sleepy feeling," great weakness across the small of the back, and some swelling of the ankles.

The examination of the liver, skin, and urine revealed practically the same features as on the first admission. The urine contained from 4 to 6 per cent. of sugar, and there were quite marked reactions for acetone and diacetic acid. He was discharged on January 13, feeling about the same as on admission.

Observation Outside the Hospital. After leaving the hospital, I was able to follow the course of the disease. The patient progressively failed. His main complaint was drowsiness and great weakness in the lumbar region. His disposition changed and he would at times have violent fits of anger. The reactions for acetone and diacetic acid became very intense and persisted for a long time, even with large doses of sodium bicarbonate. Small amounts of carbohydrates were permitted daily. During the night of February 11, he had a chill and the temperature rose to 100.2° F. The next day patches of bronchopneumonia were detected over the lower lobe of the left lung. Fearing the onset of coma the sodium bicarbonate was increased to 4 grams every two hours and the patient was put on a diet of eggs, with a quart of milk and a half-pint of cream daily.

On February 14, contrary to expectation, the reactions for acetone and diacetic acid had entirely disappeared. There was 2.4 per cent. of sugar present. The physical signs of bronchopneumonia were apparent. The pulse was 132 and much weaker. The respirations were 32 to the minute, but had no suggestion of an "air-hunger" type. Although the patient was dull this seemed to be due rather to his general weakness than to advancing coma. He died suddenly at 12.10 A.M. on February 15. Every effort was made to secure an autopsy, but the patient's family refused permission.

It was most unfortunate that autopsies could not be obtained in these two cases. Both patients died after leaving the hospital. I fully appreciate the risk in making a diagnosis of hemochromatosis without the evidences afforded by an autopsy. Personally I am fully convinced that both were cases of diabetes due to hemochromatosis. Each possessed the triad of symptoms characteristic of hemochromatosis in its final stage: pigmentation of the skin, hypertrophic cirrhosis of the liver, and diabetes of a severe type. Even with this symptom-complex one would hesitate to make a diagnosis of hemochromatosis without the finding of iron in the skin. In both these cases, however, hemosiderin was demonstrated in the epithelial cells of the sweat glands, in the first case by Dr. Opie, and in the second case by Dr. Bunting. I have, therefore, little hesitation in placing these two cases on record as instances of diabetes due to hemochromatosis.

In neither case was there any demonstrable evidence of blood destruction. In each the blood count was practically normal. In Case II the blood was examined spectroscopically for abnormal absorption bands, and the urine by the same means for hematoporphyrin with negative results. The only evidence of possible blood or vascular changes was in Case I, in the existence of a few small purpuric spots about one of the ankles. In Case I it was impossible to determine the relationship of the time of the onset of the skin pigmentation to the liver changes and diabetes. In Case II, however, the pigmentation undoubtedly antedated the diabetic symptoms which had existed for only six months before death. The skin pigmentation, having existed for as long as members of his family could remember, presumably also antedated the hypertrophic cirrhosis of the liver.

Before preceding to a brief consideration of the pathogenesis of hemochromatosis, I shall give a very brief summary of the cases of this disease associated with diabetes mellitus that have been reported since the appearance of the paper by Anschütz in 1899. The names of the observers and a brief synopsis of the cases follow:

I. Henry W. Berg.[6] Female; aged forty-four years; pigmented skin; exophthalmic goitre; enlarged liver; diabetes. Patient alive when reported. Skin not examined for iron.

II. A. Murri.[7] Female, aged fifty-nine years; pigmentation of arms; pediculi present; liver and spleen not enlarged. Highest percentage of sugar 4.3. Patient discharged "well." Skin not examined for iron.

III. K. Ubert.[8] Male; physician; age not given; 7 per cent. of sugar; enlarged liver and spleen. Death from coma. Diagnosis confirmed at autopsy.

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[6] Med. Record, 1899, vol. lvi, p. 881.

[7] Wiener klinische Rundschau, vol. xv, p. 345.

[8] Dissertation. Ueber Hemochromatolyse mit Pankreasatrophic und Diabetes (Zurich) Affoltern, 1902, J. Weiss.

IV. R. Lepine.[9] Male; aged forty-five years; 71 grams sugar in twenty-four hours; diabetes lasted eight months; enlarged liver and spleen; diagnosis confirmed at autopsy.

V. J. W. Beattie.[10] Male; aged thirty-nine years; pigmentation of the skin, which was thought to have followed the diabetes; death from coma; pigmentary cirrhosis of the liver and pancreas found at autopsy.

VI. L. Margain.[11] Male; aged forty-seven years; pigmentation of skin; relationship of onset of pigmentation to onset of diabetes not determined; enlarged liver. Autopsy.

VII. Hess and Zurhelle.[12] Case I. Male; aged fifty-two years; pigmentation of skin; diabetes; autopsy, showing hypertrophic pigmentary cirrhosis of the liver and sclerosis of the pancreas with pigmentation.

VIII. Hess and Zurhelle.[13] Case II. Male; aged fifty-three years; marked alcoholic; pigmented skin; severe diabetes; autopsy, showing hypertrophic cirrhosis of the liver and a pigmented, firm pancreas.

IX. G. H. Moll van Charante.[14] Male; aged thirty-two years; skin pigmentation; enlarged liver; severe diabetes; death from coma; autopsy, showing general hemochromatosis.

In 1882, Hanot and Chauffard first described two cases of diabetes mellitus associated with hypertrophic cirrhosis of the liver and a bronze-like pigmentation of the skin. Four years later Lettulle reported two similar cases. In 1886, Hanot and Schachmann reported a fifth case. As all these cases agreed in that there was diabetes, a pigmentary hypertrophic cirrhosis of the liver, and, with the exception of Hanot and Schachmann's case, pigmentation also of the skin, the latter clinicians felt that they had established the existence of a new form of cirrhosis, *cirrhose pigmentaire diabètique*, as well as a new form of diabetes, *diabète bronzé.*

The majority of French clinicians have held that the diabetes is primary; that the diabetic alteration of the blood causes a destruction of the red cells, with the deposition of the blood pigment in the viscera and in the skin, giving rise to the so-called bronzed diabetes.

When von Recklinghausen, in 1899, described a general pigmentation of the viscera under the name of "hemochromatosis," it became at once apparent that this condition was closely related to bronzed diabetes. von Recklinghausen found that the tissues in hemochromatosis contained two varieties of pigment. One of these, "hemosiderin," contains iron, and possesses a brown color, and is thought to be derived from the hemoglobin of the blood. It is found in the cells of the lymphatic glands, liver, pancreas, and the sweat glands. The other, "hemofuscin," contains no iron, is finer, of an ochre-yellow color, and is present in the smooth muscle cells of the stomach, intestines, bloodvessels, and lymphvessels, but rarely in those of the urinary bladder, ureter, and vas deferens. It is also found in the connective-tissue cells of certain localities—for example, Glisson's capsule, the trabeculæ of the spleen, and the sheaths of the bloodvessels.

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[9] Lyon médical, 1903, vol. c, pp. 593 and 652.

[10] Journ. of Path. and Bact., 1903-1904, vol. ix. p. 117.

[11] Revue de Médecine, 1905, vol. xxv, p. 214.

[12] Zeitschrift f. klinische Medizin, 1905, vol. lvii, p. 344.

[13] Ibid.

[14] Neiderl. Tijdschr. v. Geneeskunde, Amst., 1905, vol. xli, p. 1727.

As more cases of hemochromatosis were studied, the view gained ground that in this condition some unknown agent caused an increased vulnerability of the red cells with dissolution of the hemoglobin and deposition of the two pigments in the situations already noted. The deposition of the hemosiderin in the cells of the liver and pancreas and of the hemofuscin in the connective tissue of these glands eventually leads to the large, cirrhotic, pigmented liver and the sclerotic pigmented pancreas which are so characteristic of the disease. The general belief now is that diabetes develops in hemochromatosis only when the pancreatic tissue becomes so seriously diseased that the islands of Langerhans are largely destroyed. The glycolytic ferment, which is supposed to be formed in these islands, is no longer produced and is not able to render active, according to Cohnheim, another ferment-like body produced in the muscles, a function which, according to this observer, is necessary for the proper utilization of the carbohydrates. Consequently, an accumulation of glucose results, a hyperglycemia occurs, and permanent diabetes ensues. The diabetes is of a severe grade and dominates the picture in the late stages of the disease. Acidosis is nearly always present and the majority of patients die of diabetic coma. Death usually occurs within one year after the onset of the diabetic symptoms, although it was deferred for twenty months in the first case here reported.

As to the relationship of the diabetes to the pigmentation the above view is the one generally held. The pigmentation of the viscera is primary and antedates the diabetes. The skin is not always pigmented in hemochromatosis. There may be visceral pigmentation long before there is any bronzing of the skin. The view formerly strongly supported by the French clinicians that the diabetes is primary and responsible for the pigmentation and visceral changes has now few adherents.

The basal cause of hemochromatosis still remains an unsolved problem. The view generally held is that some unknown toxic agent causes an increased hemocytolysis of the red cells. In a few of the reported cases there has been some evidence to support this view, such as the rare occurrence of purpura and the existence of hemoglobinuria in Case II of Hess and Zurhelle. On the other hand, Meltzer[15] has suggested that the absence of any anemia in these cases is strongly against the view that there is increased blood destruction in hemochromatosis. In a discussion of Berg's case he cites the fact that there is an absence of general hemochromatosis in pernicious anemia, in which there is increased blood destruction, as an argument against the view that hemochromatosis is due to a pathological condition of the red cells. He is inclined to think that the excess of iron in the tissues is due to a disturbance of the mechanism of metabolism which has to do with the removal of iron from the system. In other words, there may be an iron retention. As the amount of iron eliminated in the feces about equals that absorbed by the system from the food, he thinks that some light may be thrown on the subject by a quantitative analysis of the iron excreted in the stools.

The most thorough pathological and chemical study of hemochromatosis in recent years is that by Hess and Zurhelle. They strongly support the view that the cirrhosis of the liver and the pigmentation of the tissues are dependent on some common cause. They hold that some toxic substance, possibly alcohol, causes disturbances of metabolism which bring about both of the above changes. A lipemia, which was present in one of their cases, is explained in the same way. Their investigations also go to show that a sharp distinction between hemosiderin and hemofuscin cannot be made. They claim to have found them side by side in the same cell with gradual transitions from one to the other.

Of the thirty-five recorded cases of bronzed diabetes, including the two here reported, all but two were in males. These two have been reported since Anschütz's analysis of twenty-four cases in 1899, at which date he found that all the reported cases were in males. Cases in women have been reported by Berg, of New York, and Murri, of Bologno. The records of these cases, however, leave a doubt in one's mind as to whether they were true cases of bronzed diabetes. Neither came to autopsy and there is no report of iron having been examined for in the skin. It may be mentioned here that a case of hemochromatosis in a female was reported by Dr. Maude Abbott. As this patient did not have diabetes it has not been included in this series. The ages of the patients ranged from thirty to sixty years, with the exception of one patient who was sixty-one. The diabetes, as already stated, is the final stage of the disease and is in no special sense different from other cases of this affection. It is of a severe form and almost invariably causes death from coma within one year after its onset.

SUMMARY. Hemochromatosis with diabetes mellitus (bronzed diabetes) is a rare disease. Of 256 cases of diabetes, out of a total of 106,000 medical admissions to the wards and dispensary of the Johns Hopkins Hospital, two were due to hemochromatosis. Of thirty-five cases in the literature, including the two here reported, all but two were in males. With one exception the ages of the patient ranged from thirty to sixty years.

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[15] Medical Record, 1900, vol. lvii, p. 43.

Hemochromatosis in its final stages presents a triad of symptoms: (1) Pigmentation of the viscera and, in the vast majority of cases, also of the skin; (2) hypertrophic cirrhosis of the liver—very occasionally atrophic cirrhosis; and (3) diabetes mellitus, a terminal feature, due to a sclerosis of the pancreas causing destruction of the islands of Langerhans and consequent interference with the secretion of the normal glycolytic ferment.

Death usually occurs within a year after the onset of the diabetic symptoms, although it was delayed till twenty months in Case I, herewith reported.

The balance of opinion is in favor of the view that hemochromatosis is due to some toxic agent of unknown character and origin, which results in an increased destruction of the red blood cells with deposition of hemosiderin and hemofuscin in the body tissues. Whether the changes in the liver and pancreas are due to the deposition of the pigment or to the same toxic agent which is supposed to cause the blood destruction is still a disputed question. It has been suggested that the excessive amount of iron in the tissues may be due to defective elimination rather than to increased formation from the blood.

ACUTE PULMONARY ŒDEMA, WITH SPECIAL REFERENCE TO A RECURRENT FORM.[1]

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The œdema of the lungs to which I desire to call attention is not that so commonly seen in the period of lost compensation of valvular or muscular heart disease, in cachectic states, in grave infectious diseases, or in acute and chronic nephritis in the terminal phase. It bears no relation to subcutaneous dropsy, and in typical cases is not associated with it. In the suddenness of its onset, in the alarming character of its symptoms, and in the mortal peril in which it places the patient, acute pulmonary œdema resembles angina pectoris, and deserves, with equal propriety, a separate place in our text-books. Those who, interested in the subject, look through

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[1] Read in abstract at the meeting of the Association of American Physicians, Washington, D. C., May 15 and 16, 1906.